

Countering Anthrax: Vaccines and Immunoglobulins

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Anthrax spores rank as the leading threat among bioweapons. This article reviews the accumulated evidence for immunization, either active or passive, to counter the malicious release of anthrax spores. The key protective factor in current anthrax vaccines for humans is a protein called protective antigen, which allows ingress of toxins into cells. The US vaccine is licensed to prevent anthrax, regardless of the route of exposure. Its dosing schedule is cumbersome and somewhat painful (shortcomings that may be resolved by ongoing clinical studies). It can be prescribed with the confidence commensurate with dozens of human safety studies and experience in 1.8 million recent vaccinees. For post-exposure prophylaxis, combining antibiotic prophylaxis and active immunization before illness onset may offer the best combination of prompt and sustained protection, especially for people who inhale large doses of spores. To treat anthrax infection, passive immunization using a polyclonal or monoclonal antibody product may offer important clinical benefit, especially if the anthrax bacteria are resistant to multiple antibiotics.

Although anthrax spore attacks along the eastern United States in the fall of 2001 focused attention on vulnerabilities [1], efforts to counter bioweapons are not new. Indeed, the Epidemic Intelligence Service of the Centers for Disease Control and Prevention (CDC) was formed to strengthen homeland defenses, speeding detection of natural and malicious biological incidents [2].

The intelligence community and civilian experts consistently rank anthrax spores as the leading bioweapon threat on the basis of its stability and ease of dispersion [3]. An accident at a Soviet bioweapons facility in Sverdlovsk, Russia, in 1979 killed at least 66 people, as well as livestock that were exposed to a microbial aerosol up to 50 km downwind [4]. Iraq admitted to the United Nations in 1995 that it fielded weapons containing *Bacillus anthracis* spores.

Immunization, either active or passive, is pivotal in countering the malicious use of anthrax spores as weapons. The evidence base for anthrax vaccine efficacy and safety has accumulated over recent decades. The literature on anthrax antibodies is both old and new. This article reviews the data for

both modes of immunization and suggests how to apply them clinically.

BACTERIOLOGY AND EPIDEMIOLOGY

Anthrax primarily affects herbivores [5–8]. In the 1870s, Robert Koch cultured *B. anthracis* and first demonstrated the microbial etiology of an infectious disease. *B. anthracis* is a large, gram-positive, spore-forming, nonmotile bacillus. Anthrax spores resist environmental extremes and can survive for decades in certain soil conditions.

The pathogenic determinants of *B. anthracis* are the bacterial capsule and 2 distinct protein exotoxins [6]. Anthrax toxins are unusual in that the 2 toxins share the same binding protein, called protective antigen (PA). PA combined with a protein called lethal factor constitutes the anthrax lethal toxin. The same PA molecule combined with a protein called edema factor constitutes the edema toxin. Each protein appears to lack biological activity individually.

From the mid-1800s to the early 1900s, human cases of cutaneous and inhalational industrial anthrax involved rag pickers and wool sorters [5, 6, 8]. Today, anthrax occurs primarily in Asia and Africa, via contact with domestic animals or their products (e.g., hair, wool, hides, bones, and meat).

Human anthrax cases have occurred throughout the United States, decreasing during the twentieth century as hygiene improved and the textile industry converted to synthetic fibers [6, 8]. Among 235 human cases reported from 1955 through

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2000, 224 involved cutaneous lesions, and 11 were inhalational cases.

In September 2001, a Florida man developed inhalational anthrax, the first US case since 1976 [1]. Although he was initially considered to have an isolated case, this patient led to a series of 11 confirmed inhalational cases (5 of which were fatal) plus 7 confirmed and 4 suspected cutaneous cases in Florida, New York, New Jersey, the District of Columbia, and Connecticut. Exposures were the result of contact with contaminated letters or packages or working in buildings with high-speed mail-sorting machines or occurred via contaminated environments [1, 3, 7].

CLINICAL DISEASE

Anthrax manifests in humans in 3 forms: cutaneous, inhalational, and gastrointestinal [6–11]. Infection begins when spores are introduced through skin or mucosa. Meningitis may complicate any of the 3 forms or, very rarely, present without evidence of other organ involvement. Detailed descriptions of clinical manifestations appear elsewhere in the literature.

Cutaneous anthrax results from spores that enter through skin breaches and then germinate into vegetative bacilli [6–10]. The toxins produce edema and tissue necrosis. Unrestrained, the bacilli spread to the draining regional lymph node, inducing hemorrhagic, edematous, and necrotic lymphadenitis. From nodes, bacteria enter the bloodstream and produce a systemic infection. Mortality among individuals with untreated cutaneous cases is ~20%, reduced to <1% with appropriate antibiotic therapy.

In inhalational anthrax, spores inhaled into the lungs are ingested by alveolar macrophages and transported to tracheobronchial and mediastinal lymph nodes, where they germinate [5–11]. Bacilli then spread through the blood, causing septicemia and, in approximately one-half of the cases, meningitis that may be hemorrhagic. Widening of the mediastinum visible on radiographic examination of the chest is common, as are pleural effusions that may be hemorrhagic. Shock may develop terminally; death usually occurs within 24 h after respiratory distress begins. Inhalational anthrax is almost 100% fatal if untreated. The case-fatality rate among individuals who received intensive care in the 2001 attacks was 45%.

Symptoms of gastrointestinal anthrax develop 2–5 days after eating contaminated meat [5–10]. The initial symptoms include nausea, vomiting, anorexia, and fever, followed by abdominal pain and diarrhea, which may be bloody. Sepsis with toxemia, shock, and death often develops. Gastrointestinal cases, if untreated, are associated with a mortality rate of 25%–75%.

ACTIVE IMMUNIZATION

In 1881, Pasteur attenuated *B. anthracis* and conducted a field test of his vaccine for livestock; at approximately the same time,

Greenfield performed similar work [12, 13]. Sterne developed live, attenuated strains (“live-spore vaccines”) in the 1930s, which are still used worldwide to immunize domesticated animals [5, 6]. Russian and Chinese investigators used this approach for both veterinary and human vaccines.

The major antigen in bacterial culture supernatants is PA, although smaller amounts of edema factor and lethal factor may be present [5, 6, 8, 14–16]. PA alone, in the absence of edema factor, lethal factor, or other anthrax proteins, protects animals against experimental infection.

In the United States and the United Kingdom, human anthrax vaccines consist of proteins isolated from anthrax cultures. In 1946, Gladstone demonstrated that the PA component of anthrax cultures was an effective vaccine [12, 16], leading to the current British vaccine (anthrax vaccine precipitated, produced by the Defence Science and Technology Laboratory at Porton Down) [6, 13].

Wright and colleagues used similar techniques at Fort Detrick, Maryland, to develop the precursors to the current American vaccine [6, 8, 14–17]. Brachman and colleagues conducted a controlled field trial evaluating Wright’s vaccine in the late 1950s, which was a somewhat less potent vaccine than the current vaccine [14–18]. This trial involved workers in 4 mills in the northeastern United States who processed raw imported goat hair that was contaminated with *B. anthracis* spores. Vaccine, compared with placebo, reduced the risk of anthrax by 92.5% (95% CI, 65%–100%), combining the cutaneous and inhalational cases. No isolated assessment of the effectiveness of vaccine against inhalational anthrax could be made, because there were only 5 cases. Notably, all 5 inhalational cases occurred in unimmunized people, and no cases occurred in vaccinees [18].

No controlled human efficacy trials of the current vaccine were performed, because regulators considered the differences between Brachman’s PA-based vaccine and the current vaccine to be minimal [14, 15]. The current vaccine was licensed in the United States in November 1970 for production at facilities owned by the State of Michigan. Those facilities were purchased by BioPort Corporation in 1998 and are now owned by Emergent BioSolutions. Known as anthrax vaccine adsorbed (BioThrax), it was the first modern acellular bacterial vaccine, manufactured from sterile filtrates of microaerophilic cultures of an attenuated strain (table 1).

The licensed 6-dose vaccination schedule for anthrax vaccine adsorbed is cumbersome [8, 14]. Based on antibody kinetics and safety data from small studies [19, 20], an ongoing CDC clinical trial assessing intramuscular administration and administration of fewer doses may provide evidence for less painful administration, comparable immunogenicity, and a simpler schedule. For those with a continued risk of exposure, additional yearly booster doses are currently recommended, al-

Table 1. Characteristics of anthrax vaccine licensed by the US Food and Drug Administration.

Variable	Characteristic
Generic name	Anthrax vaccine adsorbed
Brand name	BioThrax
Synonyms	ANT, AVA
Manufacturer	Emergent BioSolutions
License status	Licensed by US Food and Drug Administration since 1970
Viability	Bacterial subunit vaccine
Indication	To prevent infection due to <i>Bacillus anthracis</i>
Strain	V770-NP1-R
Concentration	5–20 mcg/mL protein, $\geq 35\%$ protective antigen
Adjuvant	Aluminum hydroxide, 0.8–1.5 mg aluminum per mL
Preservative	Benzethonium chloride, 0.0025%; formaldehyde, $<0.02\%$
Production medium	Synthetic medium
Dosage form	Suspension
Solvent	Isotonic sodium chloride
Packaging	10-dose, 5-mL vial
Routine storage	Refrigerated at 2°–8°C
Dosage, route	0.5 mL administered subcutaneously over the deltoid region

NOTE. The standard schedule is 6 doses administered at 0, 2, and 4 weeks and at 6, 12, and 18 months, plus annual boosters.

though the possibility of extending booster intervals is also under study.

Modern experiments show that the licensed vaccine protected 62 (95%) of 65 rhesus monkeys and 114 (97%) of 117 rabbits against lethal aerosol challenge with anthrax spores (tables 2 and 3) [14, 21–26]. A comprehensive, peer-reviewed evaluation by the National Academy of Sciences reported: “The committee finds that the available evidence from studies with humans and animals, coupled with reasonable assumptions of analogy, shows that anthrax vaccine adsorbed as licensed is an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by all known or plausible engineered strains of *B. anthracis*” [14, p. 10].

In an anthrax attack, postexposure vaccination, by itself, is unlikely to provide protection, because the disease has a short incubation period and a rapid course. However, a combination of treatment with antibiotics and active immunization between exposure and illness onset may offer the best combination of prompt and sustained protection against inhalational anthrax [3, 7, 8, 14]. Antibiotics would protect acutely against infection, giving the vaccine time to elicit active immunity. This approach is analogous to postexposure therapy for rabies, where rabies immunoglobulin protects acutely during the period in which rabies vaccine induces active immunity [27].

Postexposure vaccination may shorten the period of antibiotic prophylaxis required [3, 7, 8, 14, 28]. In animal studies, viable spores persisted for weeks to months within the lungs of rhesus monkeys after inhalational challenge, at which time, some spores could still germinate and cause fatal infection [28–

31]. This suggests that people who inhale large doses of spores may be most likely to benefit from the prolonged prophylaxis afforded by active immunization, in contrast with the finite duration of prophylaxis provided by antibiotics. Unfortunately, there is no effective method to quantify the number of anthrax spores inhaled outside of experimental settings.

VACCINE SAFETY

A contraindication to any vaccination is a prior hypersensitivity reaction to the vaccine. Severe injection-site reactions or systemic reactions have occurred with the licensed vaccine. If it is necessary to immunize individuals with prior hypersensitivity reactions, pretreatment with antihistamines and nonsteroidal anti-inflammatory drugs may be of value, although this has not been evaluated formally [8].

An estimated 150,000 American military personnel received 1 or 2 anthrax vaccinations during the Persian Gulf War in 1991, but individual records were either not kept (in an attempt not to identify those individuals who were not vaccinated and, therefore, were vulnerable to enemy bioweapons) or were marked with terms such as “vaccine A” [8, 14, 17]. In March 1998, a much larger vaccination program began that has now administered >6.8 million anthrax vaccinations to >1.8 million personnel. Anthrax vaccinations are primarily intended for military personnel serving in areas judged to be at higher risk (e.g., southwest Asia and Korea), as well as for personnel with homeland biodefense roles.

From 1998 through 2001, anthrax vaccine was the target of

Table 2. Protection of rhesus macaques by the licensed anthrax vaccine adsorbed against lethal aerosol *Bacillus anthracis* spore challenge.

Study group	No. of anthrax vaccine adsorbed doses	Vaccine dose	Route of vaccination	Vaccination schedule, weeks	Challenge point, ^a weeks	Spore challenge, mean LD ₅₀	Challenge <i>B. anthracis</i> strain	No. of survivors/total vaccinated subjects ^b	No. of survivors/total unvaccinated subjects ^c	Reference(s)
1	2	0.5 mL	SC	0, 2	8	437	Ames	10/10	0/5	[21, 22]
2	2	0.5 mL	SC	0, 2	38	203	Ames	3/3	...	[21, 22]
3	2	0.5 mL	SC	0, 2	100	330	Ames	7/8	0/2	[21, 22]
4	2	0.5 mL	IM	0, 4	16	899	Ames	9/9	0/2	[23]
5	2	0.5 mL	IM	0, 4	16	138 or 155	Ames	5/5	0/6	[23]
6	1	0.5 mL	IM	0	6	74	Ames	10/10	0/3	[24]
7	2	0.5 mL	IM	0, 4	10	398 ^d	Namibia ^e	10/10	0/2	[25]
8	2	0.5 mL	IM	0, 4	10	1004 ^d	Turkey ^e	8/10	0/2	[25]

NOTE. IM, intramuscular injection; LD, lethal dose; SC, subcutaneous injection.

^a Weeks to challenge time is calculated from the first vaccine dose.

^b Overall, a total of 62 (95%) of 65 vaccinated subjects survived.

^c Overall, a total of 0 (0%) of 22 unvaccinated subjects survived.

^d LD₅₀ challenges values for geographically diverse strains are Ames LD₅₀ equivalents.

^e Geographically diverse strains are designated by the country of origin.

prolonged skepticism, evoking the National Academy of Sciences review and an extraordinary array of postlicensing safety studies [14, 32–41]. These studies involved cohort studies of acute symptoms, hospitalizations, disability evaluations, and reproductive outcomes, as well as secondary review of spontaneous reports to the Vaccine Adverse Event Reporting System. Follow-up intervals in these studies ranged from months to decades.

Public concerns about health problems associated with anthrax vaccination encompassed so many diverse diagnoses (e.g., lupus erythematosus, hypothyroidism, diabetes, cancers, Guillain-Barré syndrome, and multiple sclerosis) that epidemiologists conducted objective comparisons of anthrax-vaccinated and unvaccinated personnel for each major diagnostic group [14, 35]. The objective comparisons showed that the vaccinated and unvaccinated cohorts had comparable rates of illness and health. Many of the individual concerns can now be understood as instances of the post hoc ergo propter hoc fallacy.

Recognition in 1999 that women who had received the anthrax vaccine experienced transient injection-site symptoms and other adverse events more frequently than men who had received the anthrax vaccine was one of the first indications of a sex differential of this type [14, 32–34]. Of interest, a retrospective analysis by the CDC of prelicensing data has shown that the sex differential also occurred in the 1960s, although it was unrecognized at that time [42]. More recently, analyses of meningococcal vaccinees, tetanus-diphtheria-pertussis vaccinees, and other vaccinees have shown similar sex differentials.

After the National Academy of Sciences heard from anthrax vaccinees and comprehensively reviewed the accumulated scientific data, it concluded that anthrax vaccine has an adverse reaction profile that is similar to that of other adult vaccines

[14]. However, injecting this vaccine adjuvanted with aluminum hydroxide by the licensed subcutaneous route of administration causes an elevated rate of injection site pain (including a burning sensation lasting ~1 min) and swelling, occasionally with peripheral neuropathy from pinching of the ulnar nerve [40]. Therefore, anthrax vaccine should be administered over the deltoid region, not the triceps region. The CDC is conducting studies to further evaluate rare adverse events (e.g., prolonged myalgia and arthralgia) and the relative effectiveness of intramuscular injection with regard to immunogenicity and safety [17].

Reports of the early experience with PA-based vaccines identified adverse event rates that are remarkably low by contemporary standards [27]. For decades, the vaccine's prescribing information cited systemic adverse event rates of 0.2%, based on CDC data [15, 42]. Investigators and clinicians reporting from occupational health clinics likely tended to omit mild, self-limited events. When the same vaccine was administered in conjunction with modern survey methods in military settings during the period 1998–2000, adverse event frequencies were obtained that were similar to those for other licensed vaccines, and these adverse event frequencies are now reflected in prescribing information [14, 32–34, 39, 41].

Safety studies involving anthrax vaccine were critically reviewed by a civilian expert committee convened by the National Academy of Sciences. The peer-reviewed report concluded that the licensed anthrax vaccine has a side-effect profile that is similar to that for other adult vaccines. According to the reviewers, "The committee found no evidence that people face an increased risk of experiencing life-threatening or permanently disabling adverse events immediately after receiving anthrax vaccine adsorbed, when compared with the general pop-

Table 3. Protection of New Zealand white rabbits by the licensed anthrax vaccine adsorbed against lethal aerosol *Bacillus anthracis* spore challenge.

Study group	No. of anthrax vaccine adsorbed doses	Vaccine dose	Route of vaccination	Vaccination schedule, weeks	Challenge point, ^a weeks	Spore challenge, mean LD ₅₀	Challenge <i>B. anthracis</i> strain	No. of survivors/total vaccinated subjects ^b	No. of survivors/total unvaccinated subjects ^c	Reference
1	2	0.5 mL	IM	0, 4	16	63	Ames	9/10	0/10	[14]
2	2	0.5 mL	IM	0, 2	8	130	Ames	10/10	0/8	[14]
3	2	0.5 mL	IM	0, 4	10	133	Ames	8/8	...	[26]
4	2	One-quarter dilution	IM	0, 4	10	133	Ames	10/10	...	[26]
5	2	0.5 mL	IM	0, 4	10	84	Ames	10/10	0/10	[26]
6	2	One-quarter dilution	IM	0, 4	10	84	Ames	10/10	...	[26]
7	2	0.5 mL	IM	0, 4	10	1305 ^d	Namibi ^e	9/10	0/10	[25]
8	2	0.5 mL	IM	0, 4	10	1448 ^d	India ^e	9/9	0/10	[25]
9	2	0.5 mL	IM	0, 4	10	360 ^d	Norway ^e	9/10	0/10	[25]
10	2	0.5 mL	IM	0, 4	10	1191 ^d	France ^e	10/10	0/10	[25]
11	2	0.5 mL	IM	0, 4	10	790 ^d	Turkey ^e	10/10	0/10	[25]
12	2	0.5 mL	IM	0, 4	10	2743 ^d	Indonesia ^e	10/10	0/10	[25]

NOTE. IM, intramuscular injection; LD, lethal dose.

^a Weeks to challenge time is calculated from the first vaccine dose.

^b Overall, a total of 114 (97%) of 117 vaccinated subjects survived.

^c Overall, a total of 0 (0%) of 88 unvaccinated subjects survived.

^d LD₅₀ challenges values for geographically diverse strains are Ames LD₅₀ equivalents.

^e Geographically diverse strains are designated by the country of origin.

ulation. Nor did it find any convincing evidence that people face elevated risk of developing adverse health effects over the longer term, although data are limited in this regard (as they are for all vaccines)” [14, p. 2].

Additional safety studies of anthrax vaccinees continue to be performed to assess rare events [43, 44]. But no common patterns of adverse events have been detected, other than the swelling and nodules attributable to injecting aluminum hydroxide subcutaneously [40].

PASSIVE IMMUNIZATION

In a patient ill with anthrax, it is too late for vaccination to offer protection. The principal treatment involves antibiotic therapy [1, 3, 6, 7]. Antibiotic regimens need to be altered on the basis of susceptibility testing and clinical status.

In the era before antibiotics, animal and human antisera were common immunotherapeutic products [12, 45, 46]. Among the first of these was anthrax antiserum, developed in France by Marchoux and in Italy by Sclavo in 1895. Although it was used initially for prophylaxis and treatment of anthrax among livestock, Sclavo soon used his product to treat human disease, either cutaneous or septicemic. He reported 10 deaths among 164 treated patients (6% mortality, compared with a contemporary case-fatality rate of 24%) [15]. Sclavo injected 30–40 mL of antiserum subcutaneously, repeating the dose 24 h later. In severe cases, he also injected ≥ 10 mL of antiserum intravenously.

Between the 1910s and 1940s, clinicians in Europe and America treated patients with anthrax antiserum using 25–300 mL

administered daily for 5 days [12, 45, 46]. The US Army medical supply catalog of 1943 included human anthrax antiserum. For decades, equine anthrax antiserum derived from live-spore vaccination has been licensed in China [5, 6], in the Soviet Union, and, later, in Russia. The effectiveness and frequency of its current use in these countries is unclear.

Although the importance of anthrax toxins in pathogenesis suggests that antiserum may play a role in treatment, no one has conducted controlled human studies to demonstrate the efficacy of anthrax antiserum. The product was superseded in the 1930s and 1940s by sulfanilamide, penicillin, and other antibiotics [6, 14, 46].

However, if a future bioweapon attack involves antibiotic-resistant strains of anthrax, the need for therapeutic agents other than antibiotics may be vital. Modern experimental evidence indicates that passive immunization with antiserum prevents anthrax in animals when antiserum is given before or shortly after spore challenge [6, 16]. This includes protecting guinea pigs from intradermal challenge, rhesus monkeys from low-dose aerosol challenge, and pretreated rats from parenteral challenge.

While additional passive immunization data in animal models are collected, the US Strategic National Stockpile will cache 10,000 therapeutic courses of human polyclonal anthrax immunoglobulin. This product was manufactured in the middle of this decade by fractionating the plasma of volunteers who had previously been given ≥ 4 doses of anthrax vaccine adsorbed (table 4).

Anthrax immunoglobulin formed part of the successful treat-

Table 4. Characteristics of anthrax-neutralizing antibody products.

Variable	Anthrax immunoglobulin	Raxibacumab
Brand name	None	ABthrax
Synonyms	Anthrax immunoglobulin	...
Specificity	Polyclonal	Monoclonal IgG1
Manufacturer	CanGene	Human Genome Sciences
License status	Investigational new drug	Investigational new drug
Route of administration	Intravenous	Parenteral (intramuscular and intravenous described)
Source	Human plasma	Mouse myeloma cell line
Notes	Emergent BioSolutions is also developing a polyclonal human anthrax immunoglobulin	Other monoclonal anthrax immunoglobulins in development include Anthim (Elusys Therapeutics) and Valtorim (developed via a partnership between Medarex and PharmAthene)

ment of a 2006 case of inhalational anthrax in a 44-year-old man who was exposed via African hides [47]. However, definitive evidence of efficacy in humans is currently unavailable.

FUTURE APPROACHES TO IMMUNIZATION

Biotechnologies offer the potential to provide improved anthrax vaccines. The ideal anthrax vaccine would be more completely defined and able to produce long-lasting immunity within several weeks [6, 14].

Several vaccine candidates that are based on recombinant PA protected rhesus monkeys from inhalational challenge [6, 14]. The Department of Health and Human Services contracted with VaxGen (Brisbane, California) to produce 75 million doses of a recombinant PA vaccine, but this contract was terminated in 2006 without successful production of the vaccine [48]. Another approach would develop live vaccines for human use, based on evidence that live vaccines protect experimental animals better than the licensed vaccine [6]. Scientists are also assessing vaccines that are based on other anthrax antigens, such as spore components, bacterial capsule, or antigens based on edema factor or lethal factor.

Modern technologies are also being applied to anthrax-neutralizing antibodies. The Department of Health and Human Services contracted for 20,000 treatment courses of raxibacumab (ABthrax; Human Genome Sciences), a monoclonal antibody to counter *B. anthracis* (table 4) [49]. In China, the Lanzhou Institute of Biological Products developed a lyophilized antianthrax F(ab)2 formulation of equine IgG fragments for human use by intracutaneous, intramuscular, or intravenous administration, but it is little used [6].

In conventional therapy, monoclonal antibodies may have advantages over polyclonal antibodies in antigenic specificity. But it is unclear whether, to counter bioweapons, polyclonal antibodies that neutralize several epitopes might be preferable to monoclonal antibodies that target only 1 epitope [16]. If bacteria could be reengineered to modify that single epitope, an elegant monoclonal antibody might be rendered ineffective.

DISCUSSION

If an attack with anthrax weapons occurred, postexposure anthrax vaccination would elicit durable protection during antibiotic prophylaxis. Although anthrax vaccine adsorbed has endured an unusual amount of negative publicity, the scientific basis for its safety and efficacy is sound. The Department of Health and Human Services purchased 10 million doses of it for the US Strategic National Stockpile in 2005 and 2006. Clinicians can prescribe it with the confidence commensurate with dozens of published safety studies involving 1.8 million recent vaccinees who have been administered 6.8 million vaccinations.

Special circumstances that warrant pre-exposure vaccination with anthrax vaccine are based on an occupational risk of exposure to anthrax spores, either naturally or as bioweapons. Examples include military personnel and other workers with homeland biodefense roles or decontamination roles. Those given preexposure vaccination receive protection from covert exposure and avoid adverse events associated with chemoprophylaxis.

To treat anthrax infection, passive immunization using an antibody product may offer adjunctive value to antibiotic therapy. If the anthrax bacteria were resistant to multiple antibiotics, the value of passive immunization would be even greater.

Several questions related to anthrax countermeasures remain to be addressed. Based on animal studies, anthrax-neutralizing antibodies could provide short-term prophylaxis (such as for decontamination workers), but the proper human dose has not been established. Indeed, data sufficient to license both polyclonal anthrax immunoglobulin and raxibacumab are needed.

For anthrax vaccine, the results of the CDC study of a less painful route of administration and greater dosing intervals are eagerly awaited. Pediatric studies of immunogenicity at various dosing regimens are also needed. Until then, the adult dose presumably applies, analogous to the uniform dose for tetanus toxoid [27].

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